DOI:
10.1016/j.puhe.2017.12.002

Document Version
Peer reviewed version

Abstract

Objectives: Despite promising research showing that physical activity (PA) might improve cognitive functioning in people with mild cognitive impairment (MCI), people with MCI are less physically active compared to the general population. Therefore, the aim of this study was to assess PA correlates among community-dwelling older people with MCI in six low- and middle-income countries.

Design: Cross-sectional data from the World Health Organization's Study on Global Ageing and Adult Health were analysed.

Methods: PA level was assessed by the Global Physical Activity Questionnaire. 4,854 participants with MCI (mean age 64.4 years; 55.1% females) were grouped into those who do and do not (low PA) meet the 150 minutes of moderate-to-vigorous PA per week recommendation. Associations between PA and the correlates were examined using multivariable logistic regressions.

Results: The prevalence of low PA was 27.4% (95%CI=25.0-30.0). In the multivariable analysis, older age and unemployment were the only sociodemographic correlates of low PA. The significant positive correlates of low PA in other domains included depression, being underweight, obesity, asthma, chronic lung disease, hearing problems, visual impairment, slow gait, weak grip strength, poor self-rated health, and lower levels of social cohesion.

Conclusions: The current data illustrate that a number of sociodemographic and health factors are associated with PA levels among older people with MCI. The promotion of social cohesion may increase the efficacy of public health initiatives while from a health care perspective, somatic co-morbidities, muscle strength and slow gait need to be considered when activating those at risk for dementia.

Keywords: physical activity; exercise; cognition; exercise

Introduction

With an advancing aging population and associated worldwide rise in dementia prevalence, the associated costs and disease burden have exerted significant pressure on global economic and social systems [1]. Currently, it is estimated that approximately 50 million people worldwide are diagnosed with dementia, this figure is expected to increase to 132 million by 2050 [2]. There is increasing recognition that due to an upward trend in physical inactivity and non-communicable diseases in low- and middle-income countries (LMICs) [3], both risk factors for developing dementia [4, 5], this part of the world is likely to experience the largest burden of dementia. Currently 58% of the world population having dementia lives in LMICs, but this percentage is estimated to increase to 68% in 2050 [6].

There are at the moment no proven treatments available to cure dementia or to alter its clinical course [7, 8]. Therefore, primary prevention and public health initiatives in the precursory stages of dementia is essential. Mild cognitive impairment (MCI) is considered to be a preclinical state of dementia [9]. Identifying modifiable risk factors for dementia in people with MCI is important in order to establish public and clinical health initiatives that might prevent or delay the onset of dementia. It has been demonstrated that low physical activity (PA) is such a risk factor with population attributable risk for dementia being 21.0% (95%CI=5.8-36.6), 20.3% (95%CI=5.6-35.6), and 21.8% (95%CI=6.1-37.7) in the USA, Europe and UK, respectively [10]. It is estimated that regular PA could prevent almost 300,000 cases of dementia per year, worldwide, if everyone were to comply with the public health recommendation of 150 minutes of moderate-to-vigorous PA per week [11]. There are likely cellular (e.g. neurogenesis, synaptogenesis, neuro-angiogenesis) and humoral (e.g. neurotrophic factors, inflammatory cytokines) mechanisms and behavioural and socioemotional pathways (e.g., stress, sleep, depression, pain) [12] that explain PA effects on the brain and cognition.

Despite promising research showing that PA might improve cognitive functioning in people with MCI [13-19], it is concerning that people with MCI are, compared to the general population, at a higher risk of not meeting the recommended 150 min/week moderate-to-vigorous intensity PA level (odds ratio=1.28; 95%CI=1.11-1.48) [20]. To date, there is no research investigating factors that influence PA participation in this population. Understanding the correlates of PA in MCI is important for multiple health reasons, including the enhancement of executive function[21] for the maintenance of personal autonomy[22] and reducing caregiver burden[23]. In addition to the overall lack of information on factors influencing PA participation in people with MCI, very little is known about PA correlates in older people in LMICs in general. This is important as these countries are characterized by a suboptimal treatment of neurocognitive disorders and mental health problems [24], and often a lack of

knowledge regarding the benefits of PA [25, 26]. Information on PA correlates of older people with MCI in LMICs could guide the design and delivery of targeted public health interventions in these countries. It could also provide useful information that can support integration of PA into primary health care settings in many LMICs.

Thus, given the aforementioned gaps within the literature, we aimed to assess PA correlates among community-dwelling older people with MCI in six LMICs.

Methods

The survey

Data from the Study on Global Ageing and Adult Health (SAGE) survey was analysed. This dataset is publically available through the World Health Organization (WHO) website (http://www.who.int/healthinfo/sage/en/). The survey was undertaken in China, Ghana, India, Mexico, Russia, and South Africa between 2007 and 2010. These countries were all LMICs according to the World Bank classification at the time of the survey. Details of the survey methodology have been published elsewhere [27]. Following a common research protocol across countries, trained interviewers conducted face-to-face interviews using a standard questionnaire to collect information. Standard translation procedures for the questionnaires were undertaken to ensure comparability between countries. A stadiometer and a routinely calibrated electronic weighing scale were used to measure height and weight respectively. Blood pressure was measured three times with a one-minute interval with the use of a wrist blood pressure monitor. Grip strength was measured twice for both hands with the use of the Smedley's hand dynamometer. If the participant had any surgery in the last three months or arthritis or pain in the hand/wrist/arm, grip strength was not measured for that hand. Gait speed was based on a 4-m timed walk and was measured by asking the participant to walk at a usual pace. A cane or other walking aids were allowed. The interviewer recorded the time to completion of the 4-m walk.

Respondents who were unable to undertake the interview because of limited cognitive function were not included in the analysis. The survey response rate ranged from 51% (Mexico) to 93% (China). Sampling weights were constructed to adjust for the population structure as reported by the United Nations Statistical Division. Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards. Written informed consent was obtained from all participants.

Assessments

Mild cognitive impairment

MCI was ascertained based on the recommendations of the National Institute on Aging-Alzheimer's Association [28]. We applied the identical algorithms used in previous publications using a dataset with the same survey questions to identify MCI [29, 30]. Briefly, individuals fulfilling all of the following conditions were considered to have MCI:

(a) Concern about a change in cognition: Individuals who replied 'bad' or 'very bad' to the question "How would you best describe your memory at present?" and/or those who answered 'worse' to the question "Compared to

12 months ago, would you say your memory is now better, the same or worse than it was then?" were considered to have this condition.

(b) Objective evidence of impairment in one or more cognitive domains: was based on a <-1 SD cut-off after adjustment for level of education (completed secondary or less), age, and country. Cognitive function was assessed through the following performance tests: word list immediate and delayed verbal recall from the Consortium to Establish a Registry for Alzheimer's Disease [31], which assessed learning and episodic memory; digit span forward and backwards from the Wechsler Adult Intelligence Scale [32], that evaluated attention and working memory; and the animal naming task[31], which assessed verbal fluency.

(c) Preservation of independence in functional abilities: was assessed by questions on self-reported difficulties with basic activities of daily living (ADL) in the past 30 days [33]. Specific questions were: "How much difficulty did you have in getting dressed?" and "How much difficulty did you have with eating (including cutting up your food)?". If the individual reported that ADL was intact or minimally impaired based on both questions, their ADL was considered to be preserved.

(d) No dementia: Individuals with a level of cognitive impairment severe enough to preclude the possibility to undertake the survey were not included in the current study.

Physical activity (PA)

Level of PA was assessed with the Global Physical Activity Questionnaire [34]. The total amount of moderate to vigorous PA in a typical week was calculated based on self-report. Those scoring ≥150 minutes of moderate to high intensity PA were classified as meeting the recommended guidelines (coded=0), and those scoring <150 minutes (low PA) were classified as not meeting the recommended guidelines (coded=1) [35].

Sociodemographic variables

These included age, sex, highest level of education achieved (completed secondary or less), wealth, marital status (married/cohabiting or else), household size (1, 2, ≥3), setting (urban or rural), and employment status (engaged in paid work ≥2 days in last 7 days: Yes/No). Wealth quintiles were created based on country-specific income.

Health behaviour

These comprised of current drinking [alcohol use in the past 30 days (Yes/No)], fruit and vegetable intake [≥2 (fruits) and ≥3 (vegetables) servings per day (adequate)] [36], and smoking (never, current, quit) [37].

Mental health

Anxiety was defined as having severe or extreme problems with worry or anxiety in the last 30 days [38]. Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview [39] were used for the endorsement of past 12-month DSM-IV depression [40] (Details provided in **eTable 1**). Those having severe or extreme problems with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning, were considered to have sleep problems [41].

Physical health

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, and was categorized as <18.5 (underweight), 18.5-24.9 (normal), 25.0-29.9 (overweight), and ≥30 (obese) kg/m^2. Participants who had severe or extreme bodily aches or pains in the previous 30 days were considered to have bodily pain [42]. Chronic back pain was defined as having had back pain every day during the previous 30 days [43]. Fall-related injuries in the previous 12 months were assessed with questions on the presence of bodily injury and cause [44]. The participant was considered to have hearing problems if the interviewer observed this condition. Visual impairment was defined as having extreme difficulty in seeing and recognizing a person that the participant knows across the road [45].

Diabetes and stroke were solely based on lifetime self-reported diagnosis. Hypertension was defined as having at least one of: systolic blood pressure ≥140 mmHg; diastolic blood pressure ≥90 mmHg; or self-reported diagnosis. For angina, arthritis, asthma, and chronic lung disease, the participant was considered to have the condition in the presence of self-reported diagnosis and/or symptom-based diagnosis using algorithms. Specifically, the validated Rose questionnaire was used for angina [46], and other previously validated symptom-based algorithms were used for arthritis, asthma, and chronic lung disease [47, 48] (See **eTable 2**).

Physical performance

Slow gait was defined as a gait speed of ≤1 m/sec [49]. Weak handgrip was defined as <30kg for men and <20 kg for women using the average value of the two handgrip measurements of the dominant hand [50].

Health status

Self-rated health was evaluated by the question 'In general, how would you rate your health today?' Those who answered 'bad' or 'very bad' were considered to have poor self-rated health. Self-rated health has been reported to be a valid indicator of overall health and a strong predictor of outcomes such as mortality[51].

Social cohesion

The social cohesion index was built with the modified version of Ramlagan, Peltzer, and Phaswana-Mafuya (2013)[52]. It was created based on 9 questions on the participant's involvement in community activities in the past 12 months (e.g., attended religious services, club, society, union etc.) with answer options 'never (coded=1)', 'once or twice per year (coded=2)', 'once or twice per month (coded=3)', 'once or twice per week (coded=4)', and 'daily (coded=5)' (Actual questions are shown in **eTable 3**). The answers to these questions were summed (range=9-45) and later converted to a scale ranging from 0-100 with higher scores corresponding to higher levels of social cohesion (Cronbach's α=0.78).

Statistical analysis

The statistical analysis was performed with Stata 14.1 (Stata Corp LP, College station, Texas). The analysis was restricted to individuals with MCI aged ≥50 years. The difference in sample characteristics between those with and without low PA was tested by Chi-squared tests and Student's *t*-tests for categorical and continuous variables respectively. The selection of the correlates of PA was based on past literature [53]. We conducted multivariable logistic regression analyses using the overall and country-wise samples. First, we assessed the sociodemographic correlates of PA by constructing a model which includes all the sociodemographic variables (age, sex, education, wealth, marital status, household size, setting, employment status). Next, we assessed the association between each of the other health-related correlates with low PA while adjusting for all the sociodemographic variables mentioned above. We also conducted a sensitivity analysis to assess whether the correlates of MCI are similar among those with and without MCI using the overall sample including all countries. We included an interaction term of the correlate in question and MCI to test whether the association between the correlate and low PA differs by the presence or absence of MCI. The regression analyses using the overall sample were adjusted for country by including dummy variables for each country. All variables were included in the models as categorical variables with the exception of age and social cohesion (continuous variables). The sample weighting and the complex study design were taken into account in all analyses. Results from the

regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CIs). The level of statistical significance was set at P<0.05.

Results

The prevalence of MCI in the general population aged ≥50 years was 14.8% (China 24.1%; Ghana 7.3%; India 9.1%; Mexico 16.9%; Russia 9.3%; South Africa 8.2%). A total of 4,854 individuals aged ≥50 years with MCI constituted the final sample (China n=2,802; Ghana n=307; India n=646; Mexico n=329; Russia n=473; South Africa n=297). The mean (SD) age of the sample was 64.4 (17.0) years and 55.1% were females. The prevalence of low PA was 27.4% (95%CI=25.0-30.0). In terms of the sociodemographic correlates, in the unadjusted analysis, individuals with low PA were significantly older, were part of a larger household, were more likely to live in urban areas and were unemployed, while they were also less likely to be married/cohabiting (**Table 1**). In terms of other correlates, those not meeting PA guidelines had a higher rate of non-alcohol consumption, inadequate fruit and vegetable consumption, non-smoking, depression, sleep problems, were underweight, had a high BMI, bodily pain, angina, asthma, chronic lung disease, hearing problems, stroke, visual impairment, slow gait, weak grip strength, poor self-rated health, and low levels of social cohesion (P<0.05) (**Table 2**). In the multivariable analysis, the only sociodemographic correlates significantly associated with low PA were older age and unemployment (**Table 3**). The significant positive correlates of low PA in other domains based on adjusted estimates included depression, underweight, obesity, asthma, chronic lung disease, hearing problems, visual impairment, slow gait, weak grip strength, poor self-rated health, and lower levels of social cohesion (**Table 4**). Alcohol consumption and smoking were negatively associated with low PA (P<0.05). There were some differences between the countries in terms of the correlates of low PA among those with MCI (see **eTables 4 and 5**). For example, regarding socio-demographic correlates, only Ghanaian men with MCI had higher odds for low PA. People in China who completed their secondary education had higher odds for low PA, but in Ghana, an opposite trend was observed. Wealthier people had higher odds for not complying with the PA guidelines only in Russia. As for health-related factors, some were significant correlates only in selected countries. For example, depression and chronic lung disease were significant positive correlates of low PA only in China and India, low BMI and visual impairment only in India, arthritis and asthma only in China, fall-related injuries only in Ghana, sleep problems only in Mexico, and a weak grip strength only in India and South Africa. Finally, we also assessed whether the correlates of PA differ among those with and without MCI. The results showed that the correlates were similar overall but with some differences. See **eTables 6 and 7** published as

supplementary material online attached to the electronic version of this paper. Older age, being underweight, fall-related injury, slow gait, and the presence of depression were significantly more strongly associated with not meeting PA guidelines among those with MCI (significant interaction P<0.05).

Discussion

General findings

To the best of our knowledge, the current study is the first multinational study to explore PA correlates in older people with MCI. Based on the adjusted analysis, the only sociodemographic correlates significantly associated with low PA (i.e. not complying with the recommendation of 150 min/week moderate-to-vigorous intensity PA) were older age and being unemployed. Significant correlates of low PA in other domains included lower levels of social cohesion, the presence of depression, underweight or obesity, asthma, chronic lung disease, hearing problems, visual impairment, slow gait, weak grip strength, and poor self-rated health. At the behavioural level, alcohol consumption and smoking were negatively associated with low PA. Compared to those without MCI, older age, being underweight, fall-related injury, slow gait, and the presence of depression were stronger correlates for not meeting PA guidelines among those with MCI.

We found that participants who were employed were more physically active which is perhaps unsurprising. Nonetheless, the current study adds further evidence to a recent review demonstrating that there are important health benefits of continuing to engage in meaningful occupation in people with MCI [54]. Next to the physically demanding labour, active transport to and from work might be an underlying reason for the more active lifestyle of those who work. Speculatively, employment may offer opportunities for older people to connect socially, enhance social functioning and consequently have more opportunity to be physically active [55-57]. Less social cohesion was in our study related to less likelihood of complying with the PA recommendation. Social cohesion and compliance with PA guidelines may be linked to each other in various ways [58]. At the neighbourhood level, a high level of social cohesion is associated with less crime, and low neighbourhood crime rates tend to be associated with greater PA engagement [59]. Also, socially cohesive neighbourhoods may be more likely to organize community activities that present opportunities for older people to engage in physical activities [60]. At the individual level, it is important to feel socially connected to the community because it may increase the likelihood that one will take advantage of local opportunities to engage in PA.

In our multivariable analysis increasing age was another important socio-demographic correlate of PA participation in people MCI, which is in line with the wider literature. Therefore, in preventive public health

campaigns and rehabilitation programs special attention and, if required, additional support should be given to people at the oldest ages. A possible underlying reason is that those people are at an even higher risk for chronic conditions and worse cognition scores. In terms of chronic physical conditions most previous studies in people with MCI have focused on cardio-metabolic diseases [61, 62], partly motivated by the theoretical link between cognitive decline via atherosclerosis, microvascular changes, and inflammatory processes [63]. The current study shows that in motivating people with MCI towards an active lifestyle, the presence of chronic lung diseases should be considered as a barrier. Vice versa, in people with chronic lung diseases MCI should be taken into account. For example, one in four people with COPD has MCI [64] and the presence of MCI in this population is associated with a higher risk for developing depression, which is an important barrier for complying with PA prescriptions in this population [65]. Also, older people with asthma have a higher risk for MCI [66]. The presence of hearing problems [67] and visual impairments [68] should, on their turn, be considered as important barriers for being physically active due to perceived fear or risk of injury in old people in LMICs. Stigma and discrimination associated with it may further complicate PA participation in older people in these countries [69].

The presence of chronic co-morbidities also results in a higher likelihood of experiencing pain. A recent study showed that mild to moderate pain and MCI are independently associated with poor mobility, and the presence of both was associated with the poorest status [70]. Therefore, health care professionals who encounter older adults in need of mobility rehabilitation should consider screening them for pain and MCI to better inform subsequent therapeutic interventions. Collaborative interventions that seek to reduce chronic conditions and pain and improve mobility among those who present with MCI might on its turn be an important strategy to increase PA levels.

Next to this, the present study demonstrated that a slow gait speed and low grip strength are associated with lower PA in older people with MCI. These factors may be reflecting the presence of a chronic physical illness, and the difficulty to engage in PA due to these conditions. Alternatively, the observation that a low grip strength and a slow gait, but also a low BMI was associated with less PA might be due to the fact that these are measures-of-proxy of frailty and sarcopenia (pathological loss of skeletal muscle mass and function) [71, 72]. People with MCI have a high risk for sarcopenia [73], while the presence of sarcopenia is also associated with a higher risk for developing MCI [74]. A number of recent studies have demonstrated that slow gait speed is a strong predictor of future incident cognitive decline and mortality [75, 76]. Experiencing difficulty undertaking a physical performance measure assessing gait speed may therefore be an important sign that an older person is at risk of MCI and also physically inactive. Next to this, in people with MCI a worse performance on handgrip strength

and gait speed tests is associated with a higher risk of falling [77]. Risk of falls in older people is associated with a fear of falling again and avoidance of PA and increased sedentary behaviour [78].

Next, our data demonstrate that depression should be considered as an important correlate of low PA in people with MCI. Depression is very common in people with MCI with a recent meta-analysis including 57 studies and 20 892 patients showing an overall pooled prevalence of 32% (95%CI=27%-37%) [79]. Depression is well-known barrier for complying with international PA standards. [80]. Given the evidence that depression can lead also to (further) cognitive decline [81], being physically active, despite the lack of energy and motivation and a low self-efficacy, may reduce the depressive symptoms in older people [82] and consequently enhance cognitive functioning. It is possible that PA has an indirect effect on cognitive functioning through its effect on older adults' mental health. Longitudinal mediation models are however needed to further untangle the complex relationship between PA, depression, and cognition.

Finally, while we identified some variation in the correlates across the different countries, the precise reasons for such differences and inconsistencies are not clear. For example, increasing levels of wealth were only associated with lower odds for low PA in Russia but not in other countries. One potential reason might be that in Russia, increasing levels of wealth correspond more strongly to less labor-demanding jobs, which means less occupational PA. The inconsistent patterns of sociodemographic PA correlates points to apparently contrasting socio-economic patterns of risk factors for low PA. A possible reason for the differences in health-related factors may be due to differences in access to health care and awareness about prevention and control of risk factors for low PA. More research is however needed to clarify these differences, which should inform country specific interventions.

Strengths, limitations and future research

The strength of the study includes the large sample size and the use of nationally representative samples from six countries, which comprise nearly half of the worldwide population [27]. Nevertheless, the study results should be interpreted in the light of several limitations. First, PA was measured with a self-report questionnaire, which is known to be less accurate than objective assessments [83, 84] and can overestimate PA levels [85]. Second, we did not assess cognitive deficits beyond attention/working memory, learning/episodic memory and language dysfunction which might have resulted in an underestimation of the number of people with MCI. However, it is reassuring that the prevalence of MCI in our study was within previously reported figures.[86] Third, because this was a cross-sectional study, causality cannot be inferred. Fourth, we were not able to explore differences in PA

participation in people with MCI living in urban versus rural settings in more detail. Future research could explore the role of specific environmental attributes relevant to PA on mental health populations (including those who present with MCI) in LMICs such as the availability and quality of sidewalks, pedestrian zones, bicycle facilities, and factors affecting intersection quality (e.g., crosswalks, pedestrian signals). In addition, future studies would benefit from assessing to what extent macro-level environmental factors such as food insecurity, civil conflicts, and extreme weather in LMICs are linked to physical inactivity in the older population in these countries.

Heal policy-related implications

Despite the limitations, our data provides some guidance for health policy makers. First of all, employment and or volunteering work, at least when of high quality (i.e. without stressful or adverse psychosocial work conditions) [87] may serve as an opportunity for older people to engage in meaningful PA. Thus, public interventions seeking to improve the likelihood that older people with MCI can be involved in high quality employment or volunteering work may serve as an opportunity for older people to have a valuable role in society as well as achieve recommended PA targets. The current results also suggest that also in LMICs, among older adults health campaigns should consider somatic co-morbidities, reduced muscle strength, slow gait and depression as these might be important barriers for PA. On the other hand, in older adults with somatic co-morbidities, pain, frailty or sarcopenia, cognitive impairments should be taken into account as potential barriers for a more active lifestyle. However, increasing occupational PA may not be a feasible intervention target when a shift occurs from manual jobs to service-based industries in more urbanized areas. Therefore policy makers should focus on other identified PA correlates as well. For example, our study shows that the public health policy in LMICs should focus on social cohesion in order to facilitate older people to become more active. This can be done in several ways. In neighbourhoods where only a few older residents feel that they belong to the community, PA could be increased by promoting social engagement and participation among community members by organizing social and PA activities targeting older people. In neighbourhoods where the overall level of social cohesion is already high, further benefits may be achieved by socially integrating older residents who do not already feel that they belong.

In conclusion, our data illustrate that a number of sociodemographic, physical and mental health and behavioural factors are associated with PA levels among older people with MCI in six LMICs. These findings provide guidance for future public health interventions across LMICs to help older people with MCI, who are at risk for physical inactivity, to become more active.

Acknowledgements

None.

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